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EDITORIAL

THE BLESSED PRIVILEGE OF WAITING

I STOOD beside a man the other day who stared through the crystal of the bookcase at the drab green-covered volumes of *Barton's Flora.* Outside, crisp snowflakes played merry tunes on the frozen strands of a winter wind. The earth about glistened with immaculate whiteness, and men preferred to stay close to crackling coals, so biting and chill was the weather. The man slowly lifted his gaze from the flower books and said, "Let us go botanizing, boy," and promptly from the hearts of both of us there rushed a passion that sent blood cells caroming to every peripheral corner. For we two had tasted before, the blessed privilege of field communion, and we had walked together in languid happiness through avenues of tall trees skirted with a myriad blossoms. Together we had long since learned that the Lord lingers close by His flowers, and that the open hearted can always find Him there.

But, soliloquizes a reading Thomas, how botanize when the pond where lilies live is locked in rigid iciness, and the murmuring brook whose moist banks kept sweet the violet and the modest gold-cup, runs silently through awkward rifts of sodden snow. The feathered folk have traveled far away to sing their songs to other ears, and only the chirping sparrow and the raucous crow remain behind to pick our crumbs and keep our company. The breezes of evening no longer carry on their wings the fragrance of the honey-suckle, and the warm amours of the pines, but only a chilly crispness and a smell of soot and sulphur.

But the man who said "Let us go botanizing, boy," is a Man of Hope, and his words came to being so spontaneously that I knew

Note: Written some twelve years ago, this bit of writing seemed worthy of reprinting as particularly fitting to these troublous times and to this spring, so slowly breaking.

that his eye peered through the mantle of snow and saw a dainty blossom, waiting for its day of unfolding. To him the migrating robin red breast sings only wearily on the mesquite down Mexico way, and it longs and longs and longs to come home with spring, to be once again the joyous, vigorous song bird of the Philadelphia morning.

He knows full well that the frost on the lily pond will vanish with spring. He knows that the violet beneath its snow coverlet only sleeps, and that morning will soon come when it will yawn itself into a fragrant existence. He knows also that the breeze of the evening will again carry to his soul the breath of sweet flowers; that the feathered folk who flew away will come again another day, to sing in sweeter tones than ever their God directed melodies.

For it is Faith in a return of the Flowers, Hope for health to live and enjoy them, and Love of Nature and its God-director—Faith, Hope and Love, these three—that makes it possible for this man even in the dismal days of a wintry spring to say,

"Boy, let us go out among the flowers."

IVOR GRIFFITH.

PHILADELPHIANS HONORED—One of the highlights of the Purdue University's recent convocation, at which time the university recognized the fiftieth anniversary of the School of Pharmacy, was the conferring of honorary degrees on two distinguished alumni, Dr. Charles E. Vanderkleed and Dr. Julius W. Sturmer, both of Philadelphia. Dr. Vanderkleed, a graduate with the class of 1895, is superintendent of the McNeil Laboratories in Philadelphia and is an eminent research worker in his field. Dr. Sturmer, of the class of 1891, is professor of industrial chemistry and Dean of Science at the Philadelphia College of Pharmacy and Science. The principal address was given by Dr. Edward Kremers, director of the course in pharmacy at the University of Wisconsin, on the subject, "The Contributions that the Universities of the 'Old Northwest' Have Made to Pharmaceutical Education."

ORIGINAL ARTICLES

A STUDY OF ALOES AND A QUANTITATIVE DETERMINATION OF SOME OF ITS CONSTITUENTS

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THE determination of the presence and the quantitative estimation of a definite quantity of aloes in medicinal preparations has been of concern to this laboratory for some years. A survey of the existing methods for its determination shows that there does not seem to be any satisfactory method of actually determining whether a medicinal preparation contains, for instance 4 grains of aloes per ounce, more, or less. When this material is in the presence of numerous other medicinal ingredients the situation becomes still more complicated. The assay of aloes for aloin seems fair but is unsatisfactory on preparations containing relatively small amounts of aloes.

One of the principal difficulties in the general determination of aloes is due to the fact that there are three varieties recognized: The Socotrine, from Eastern Africa and the islands off the coast of Africa. The Cape aloes from the southern part of Africa and the Curacao aloes from the West Indies, are all fairly widely separated geographically and it is a natural consequence that these should be somewhat different in character. It is not unlikely that each of these consists of one separate species of aloes which has been transplanted into the various climates.

Besides these species of aloes which are recognized by the U. S. P. there are numerous other aloes obtained from hybrids which often find their way into commerce as sophistications.

The taste and appearance of these three recognized varieties are not exactly the same and one not familiar with these drugs might say that each is an entirely different substance. There are some points of similarity and when they are made into preparations, they are surprisingly alike analytically. One point of similarity is that all species contain considerable iron and it was upon this iron content that methods for their confirmation and determination have been made. See Table I showing variation in iron content.

The determination of aloin has been one of the principal points in the evaluation of aloes. Examination and use of the aloin itself,

TABLE I

Solids and Ash content of Preparations made to contain 4 grains of Aloes per fluid ounce in diluted Alcohol. (Iron was determined on the dry Powder.)

Sample No.	Solids (21% alcohol)	Ash (21% alcohol)	Solids (40% alcohol)	Ash (40% alcohol)	Grams per 100 grams Iron as of Fe_2O_3 in dry powder
1. Socotrine	.72	.03	.81	.03	.36
2. Socotrine	.72	.01	.82	.04	.44
3. Socotrine	.69	.01	.75	.03	1.03
4. Cape	.84	.01	.83	.02	.31
5. Cape	.84	trace	.83	.02	.32
6. Cape	.84	trace	.85	.01	.31
7. Curacao	.81	.02	.82	.02	.18
8. Aloin	.07	trace	...	...	.09
9. Curacao	.84	.01	.87	.03	.14
10. Curacao	.82	.01	.81	.03	.29
11. Curacao	.80	.01	.83	.02	.09
12. Curacao	.80	.01	.84	.03	.16
13. Curacao	.83	.015	.86	.02	.27
14. Socotrine	.84	trace	.90	.01	.34
15. Curacao	.78	.01	.84	.02	.14
16. Curacao	.77	.01	.84	.02	.11
17. Socotrine	.65	.01	.77	.03	.29
18. Cape	.82	trace	.86	.01	.16
19. Cape	.83	trace	.85	.01	.12
20. Cape	.79	trace	.84	.01	.12
21. Cape	.83	trace	.87	.02	.14
22. Cape	.80	trace	.83	.01	.15
23. Curacao	.78	.01	.84	.02	.11
24. Socotrine	.62	.01	.75	.04	.27
25. Curacao	.75	.01	.82	.02	.18
26. Cape	.83	.01	.87	.01	.14
27. Aloin	.08	.01	...	...	trace
28. Aloin	.08	.01	...	...	trace

NOTE that Socotrine aloes shows the highest iron content with an average of .44 grams of Fe_2O_3 per 100 grams of drug. Cape is next with .2 grams and Curacao last with .18 grams per 100 grams.

however, shows that it is far inferior to the parent aloes in physiological properties, clearly indicating that there are some other substances present which produce most of the therapeutic effect characteristic of aloes and to which a great deal of its value is due.

There are over twenty-eight specimens of aloes used in this investigation consisting of the three recognized official U. S. P. varieties, including three samples of aloin, made into preparations containing an average U. S. P. dose per ounce in approximately 21 per cent., alcohol and the same group made up with 40 per cent. alcohol. This 21 per cent. alcohol did not dissolve all the aloes in every instance. In some cases there was only a small residue left but it was found that the residue left, after extraction with this percentage of alcohol, required much higher alcohol for complete solution and in some instances there was a residue that was entirely insoluble in water or alcohol even up to 95 per cent. strength. The amount of this material soluble in 21 per cent. and 40 per cent. strength alcohol is shown in Table I. Alcohol is actually necessary up to 40 per cent. in medicinal preparation if all the essential principles of aloes are to be retained. Although aloes is one of the most ancient of drugs still in use, having been handed down since before the Christian era, a search of the literature on the subject of aloes shows no satisfactory method of its analysis. If the aloes is not in the presence of other ingredients one can judge from the characteristic odor, taste and certain simple reactions whether the full amount is present within reasonable limits. The main constituent that has been determined is aloin, the amount varies greatly in the three different recognized aloes and even frequently has a wide range in the same variety aloes. When aloin is to be obtained commercially Curacao aloes is used, due to its higher yield of aloin. The methods of aloin determination seem very crude and some investigators and drug manufacturers along this line have frankly stated, "We are satisfied to get about one-half the aloin that is present."

The work done in the laboratory of the Bureau of Industrial Alcohol is for the purpose of making a more complete analysis so that aloes can be determined more accurately as such and in the presence of other ingredients. Experience has shown that aloin extracted from aloes has not the same medicinal equivalent of the parent drug and there are other substances such as emodins, glucosides, and resins in the aloes that seem much more active physiologically than aloin itself. The water extract of crude aloes is physiologically quite active,

TABLE II

There is listed in table below the results of analysis for nitrogen, chlorine, phosphates and sulphates determined on this dry powdered aloes.

Number	% Nitrogen	N as % Protein	% Chlorine	Phosphates as $\%P_2O_5$	Sulphate as $BaSO_4$	Sulphate as SO_4
			Socotrine Aloes.			
1	.415	2.59	.85	.158	.514	.211
2	.401	2.50	.95	.076	.392	.161
3	.503	3.14	.83	.117	.513	.211
14*	.348	2.18	.06	.055		
17	.790	4.94	.72	.076	.504	.207
24	1.000	6.28	.83	.082	.535	.220
Avr.	.622%	3.89%	.84%	.102%	.492%	.202%
			Curacao Aloes.			
7	.457	2.86	.27	.047	.428	.176
9	.422	2.64	.20	none		
10	.371	2.32	.33	none		
11	.471	2.94	.23	none		
12	.419	2.62	.17	trace		
13	.344	2.15	.32	none		
15	.389	2.43	.27	trace		
16	.371	2.32	.24	.048	.312	.128
23	.366	2.29	.28	.035	.407	.167
25	.370	2.32	.17	trace		
Avr.	.398%	2.49%	.25%	.013%	.382%	.157%
			Cape Aloes.			
4	.130	.81	.12	.038	.064	.026
5	.159	.99	.09	.070	.113	.046
6	.185	1.16	.09	.040	.211	.087
18	.156	.96	.08	.028	.095	.039
19	.155	.96	.07	.034	.069	.028
20	.147	.92	.11	.042	.147	.060
21	.178	1.11	.08	.027	.077	.032
22	.150	.94	.08	.042	.088	.036
26	.126	.79	.06	none		
Avr.	.154%	.96%	.09%	.036%	.108%	.044%
			Aloin.			
8	.112%	.70		none		
27	.038	.24		none		
28	.065	.40		none		

*Sample No. 14 due to its abnormality was suspected of being adulterated and the results of analysis were not calculated in the average.

In the table below is shown the further examination of the whole aloes drug.

No.	% Moisture	% Ash	% Ash insoluble in HCl (Practically all sand)
		SOCOTRINE.	
1	4.62	5.42	.82
2		4.52	.43
3		6.69	1.36
17	4.85	6.15	.75
24	5.54	6.21	.81
		CURACAO.	
7	4.65	2.69	.33
16	4.02	2.76	.22
23	4.50	2.48	.21
		CAPE.	
4	4.54	3.33	2.45
5		1.99	.74
6	4.71	1.58	.76
18	4.77	1.90	.91
19		1.69	.90
20		1.07	.23
21		1.00	.19
22		1.86	.92

the ether extract of this aqueous extract is also physiologically active and the water insoluble material from the crude extract is also quite active. This has been proven by experiments beyond a doubt to the satisfaction of all members of this staff working on these problems.

The emodin color reactions such as used in the articles previously published on rhubarb (1) Part I, Jour. A. Ph. A. (1930), 235-238; cascara (2) Part II, Jour. A. Ph. A. (1931), Vol. XX, No. 11, and aromatic fluid extract cascara (3) AMER. JOUR. PH. (1931), September, are useful in helping to prove whether the full amount of aloes has been used in the preparation of a standard medicinal formula. Of course there must be taken in consideration that 4 grains of dry aloes only was incorporated in each ounce of solution, while in the case of rhubarb and cascara 15 minims of U. S. P. fluid extract was used in each ounce of the finished product. For a matter of comparison Table I will show the three types of aloes made up in approximately 21 per cent. alcohol and also in 40 per cent. alcohol to the extent of 4 grains per fluid ounce.

The most satisfactory method used in the Laboratory of the Bureau of Industrial Alcohol for estimating the quantity of aloes

present in fluid extracts and other aloe preparations including medicinal preparations, containing more or less aloes is based on Borntrager reaction (*Z. Anal. Chem.* 19 (1880), 165). When the group of drugs consisting of rhubarb, cascara, frangula, senna, and aloes, whose virtues depend principally upon the resinous hydroxyanthraquinone bodies and other anthraquinone compounds in solution are made acid and are extracted with ether and the ether extract made strongly alkaline with ammonia, a red color of a certain shade is caused to develop. Application is made of this test as a basis for quantitative estimation of, for instance, aloes in medicinal preparations under examination. Under certain carefully observed conditions the depth of color extracted by the ether and color developed on the treatment with ammonia varies almost directly in proportion to the amount of aloes or other emodin-bearing drugs present. These readings are to estimate the free emodin bodies, after this a separate portion of the preparation is hydrolyzed with concentrated sulphuric acid and the same process repeated. These readings are termed total emodin readings consisting of the color due to free and combined anthraquinone bodies.

The Lovibond's tintometer is depended upon to standardize the colors developed for these comparisons. A brief description of the apparatus is as follows:

The Lovibond tintometer used in these experiments is sold by Eimer and Amend, and is an instrument by which the depth of color of liquids can be accurately measured in degrees, placed in their position in a permanent color scale and registered for reproduction at any time. It consists of a graded series of standards made of colored glasses, numbered according to their depth of color and an instrument for holding the glasses, and the object to be measured.

The yellow ether extract is poured into the 1/16 inch cell and the color matched against the yellow slides. Ten cc. of the above extract is introduced into a 100 cc. Nessler tube and 10 cc. of strong ammonia (sp. gr. 0.90) added. The mixture is shaken, stoppered and allowed to stand two or three hours. It is then diluted to 50 cc. volume and mixed. As soon as the ether portion rises to the top it is poured off and some of the red liquid poured into the 1/8 inch cell of the tintometer and carefully matched against the red tinted slides as in the manner before described.

Method for color reading—Before Hydrolysis (free emodin): Extract 25 cc. of the preparation, made acid with 2 cc. N/10 H_2O_4,

extract 5 minutes with 50 cc. of ordinary sulphuric ether in separatory funnel, draw off aqueous liquor several times as it settles and take 10 cc. of the yellow ether extract and 10 cc. of strong ammonia and place in a colorimetric tube (Nessler) mix, allow to stand about two hours. The remainder of the yellow ether extract is read in 1/16 inch cell, then make the mixture in the Nessler tube up to 50 cc. volume with water. Flick off the ether which rises to the top and read the red color in a 1/8 inch cell.

Method for color reading—After Hydrolysis (total emodin): 25 cc. of each preparation was treated in an Erlenmeyer flask with 2 cc. of concentrated sulphuric acid, shaken thoroughly and allowed to stand over night; refluxed over a steam bath for 30 minutes, using a tube condenser. Transfer the material into a separatory funnel. Shake with 50 cc. of ordinary ether for exactly five minutes, allow to settle, draw off aqueous layer, shake and again allow to settle. Again draw off the remaining aqueous material. Repeat this process until all the aqueous liquor is stripped out as completely as possible.

Take 10 cc. of the yellow ether extract and 10 cc. of strong ammonia and place in a colorimetric tube (Nessler) mix, allow to stand two hours, some of the remainder of the yellow color is read in 1/16 inch cell, then make the mixture in the Nessler tube up to 50 cc. volume with water, allow to settle, pour off the ether which rises to the top and read the red color in 1/8 inch cell.

Table III shows the color readings made by the above methods. It includes the analysis of two sets of preparations, one containing 21 per cent. alcohol and the other containing 40 per cent. alcohol, the same sample of aloes being used in the two strengths of alcohol. This table includes preparations made with U. S. P. aloes purchased from the leading drug houses in the United States.

The color readings seen in Table III were made immediately after they had been prepared, allowed to stand 24 hours and filtered. After they had been stored, tightly stoppered in dark bottles at ordinary laboratory temperatures for 15 months some of the preparations containing approximately 40 per cent. alcohol were again read after fifteen months. The readings all show an increase in all the color reactions previously found. No theories are offered for it at present, but the difference can be seen by comparing the readings below with Table III with those listed in the supplementary table below.

TABLE III

COLOR READINGS MADE ON PREPARATIONS CONTAINING FOUR GRAINS PER FLUID OUNCE OF ALOES

No.	21% Alcohol				40% Alcohol			
	Before Hydrolysis		After Hydrolysis		Before Hydrolysis		After Hydrolysis	
	Free		Total		Free		Total	
	Y 1/16" Cell	R 1/8" Cell	Y 1/16" Cell	R 1/8" Cell	Y 1/16" Cell	R 1/8" Cell	Y 1/16" Cell	R 1/8" Cell
			Socotrine Aloes					
1	2.8 Y .2 R	2.2 R 1.7 Y	2.9 Y .3 R	2.9 R 1.3 Y	5.8 Y	3.0 R 2.2 Y	5.0 Y .2 R	3.3 R 1.0 Y
2	2.2 Y .3 R	2.2 R 1.4 Y	2.9 Y .5 R	2.1 R 1.0 Y	6.0 Y	3.0 R 1.6 Y	4.6 Y .2 R	4.5 R .6 Y
3	2.0 Y .3 R	1.8 R .9 Y	2.2 Y .3 R	1.8 R .9 Y	4.4 Y	2.9 R 1.3 Y	4.2 Y .3 R	4.0 R .5 Y
14	.9 Y	1.0 R .7 Y	1.7 Y	2.0 R 1.7 Y	1.4 Y	1.15 R .80 Y	1.5 Y .12 R	1.15 R .5 Y
17	1.3 Y	1.3 R 1.0 Y	1.7 Y .2 R	1.8 R .7 Y	5.8 Y .3 R	3.7 R 1.0 Y	4.0 Y .36 R	3.2 R .78 Y
24	1.3 Y	2.5 R 1.1 Y	2.0 Y .26 R	1.9 R 1.0 Y	5.2 Y .3 R	3.62 R .9 Y	4.2 Y .3 R	4.2 R 1.1 Y
			Curacao Aloes					
7	2.0 Y .3 R	1.9 R 2.0 Y	3.2 Y .8 R	2.5 R 1.6 Y	2.2 Y .16 R	1.85 R 3.0 Y	2.6 Y .6 R	2.4 R 1.4 Y
9	3.2 Y	3.0 R 1.5 Y	3.4 Y .3 R	2.9 R 1.3 Y	6.0 Y .2 R	4.12 R 1.10 Y	6.0 Y .7 R	4.8 R .4 Y
10	2.1 Y	2.2 R 1.4 Y	2.5 Y .3 R	2.3 R 1.4 Y	4.4 Y .3 R	3.12 R .9 Y	4.8 Y .95 R	3.5 R .44 Y
11	2.8 Y	2.8 R 1.6 Y	3.2 Y .3 R	2.5 R 1.2 Y	6.8 Y .32 R	4.62 R 1.60 Y	4.2 Y .42 R	3.5 R .7 Y
12	2.8 Y	2.5 R 1.6 Y	3.3 Y .4 R	2.8 R 1.3 Y	6.6 Y .2 R	4.2 R 1.5 Y	4.6 Y .5 R	3.7 R .7 Y
13	2.2 Y	2.4 R 1.3 Y	2.9 Y .4 R	2.5 R 1.3 Y	3.9 Y .26 R	2.8 R 1.5 Y	3.9 Y .88 R	2.5 R .7 Y
15	2.2 Y	2.2 R 2.0 Y	2.6 Y .3 R	2.5 R 1.3 Y	3.4 Y .3 R	2.5 R 2.9 Y	4.2 Y .64 R	3.5 R .74 Y
16	1.8 Y	2.0 R 2.7 Y	2.5 Y .2 R	2.2 R 1.1 Y	8.6 Y .3 R	5.5 R 1.0 Y	7.6 Y .64 R	5.1 R .88 Y
23	1.3 Y	1.9 R 2.4 Y	2.5 Y .3 R	2.2 R 1.2 Y	4.4 Y .26 R	3.12 R 1.10 Y	4.6 Y .8 R	4.2 R 1.3 Y
25	1.4 Y	1.5 R 1.0 Y	1.9 Y .3 R	1.6 R 1.1 Y	6.0 Y .38 R	4.14 R 1.00 Y	5.0 Y .3 R	4.2 R 1.0 Y

Cape Aloes

4	1.2 Y .2 R	.9 R 1.3 Y	1.5 Y .4 R	1.0 R .8 Y	3.5 Y	2.2 R 1.1 Y	2.6 Y .16 R	1.9 R .3 Y
5	1.4 Y .2 R	1.0 R 1.2 Y	1.6 Y .3 R	1.0 R .7 Y	4.0 Y	2.4 R 1.0 Y	2.8 Y .2 R	2.1 R .2 Y
6	1.7 Y .3 R	1.3 R 1.0 Y	2.1 Y .3 R	1.4 R .8 Y	3.9 Y .16 R	2.5 R 1.0 Y	2.8 Y .3 R	1.2 R .7 Y
18	.9 Y	1.2 R 1.1 Y	1.6 Y .1 R	1.3 R .9 Y	3.5 Y .12 R	2.2 R 1.0 Y	2.6 Y .3 R	1.75 R .7 Y
19	1.1 Y	1.2 R 1.3 Y	1.4 Y .1 R	1.3 R .7 Y	3.2 Y .3 R	2.2 R 1.7 Y	2.6 Y .12 R	2.0 R .5 Y
20	.8 Y	1.0 R 1.2 Y	1.4 Y .2 R	1.2 R .8 Y	2.10 Y .16 R	1.5 R 1.5 Y	2.0 Y .12 R	1.3 R .5 Y
21	.9 Y	1.2 R 1.2 Y	1.7 Y .2 R	1.4 R .9 Y	3.2 Y .12 R	2.1 R 1.0 Y	2.4 Y .2 R	1.6 R .5 Y
22	.9 Y	1.2 R 1.2 Y	1.6 Y .2 R	1.4 R .8 Y	2.4 Y .12 R	1.6 R 1.9 Y	2.1 Y .2 R	1.5 R .44 Y
26	.8 Y	1.0 R 1.4 Y	.9 Y .2 R	1.0 R .9 Y	2.5 Y .12 R	1.65 R .9 Y	2.0 Y .16 R	1.75 R .60 Y

Aloin

8	1.2 Y .2 R	.3 R	1.2 Y .2 R	.3 R
27	.4 Y	None	None	None
28	.2 Y	.1 R .3 Y	None	None

SUPPLEMENT TO TABLE III

Sample No.	Variety Preparation made with 40% Alcohol	Emodin Readings Before Hydrolysis Yellow in 1/16 in. Cell	 Red in 1/8 in. Cell	 After Hydrolysis Yellow in 1/16 in. Cell	 Red in 1/8 in. Cell
4	Cape	4.6 Y .2 R	2.9 R .6 Y	3.9 Y .3 R	2.3 R
5	Cape	5.0 Y .1 R	3.0 R .5 Y	3.5 Y .3 R	2.4 R
18	Cape	4.4 Y .3 R	2.5 R .7 Y	3.2 Y .3 R	2.0 R
22	Cape	4.4 Y .2 R	2.8 R .7 Y	3.3 Y .2 R	2.3 R .2 Y
7	Curacao	9.0 Y .3 R	5.0 R .6 Y	9.4 Y .9 R	5.5 R .6 Y
23	Curacao	8.6 Y .9 R	5.5 R		

Colorimetric Emodin Analysis in Presence of Phenolphthalein—Benzyl Alcohol Method

There has been developed in the Laboratory of the Bureau of Industrial Alcohol a method which has given very satisfactory results when applied to preparations containing aloes and other emodin-bearing drugs, particularly aloes and rhubarb. The principal advantages of this method are that it can be used in the presence of phenolphthalein; one may obtain complete color reactions and the color obtained is fairly permanent, there being no perceptible change for several months. From a gravimetric standpoint, however, it is practically of no value, since the benzyl alcohol has a very high B. P. (about 200° C.) and this solvent extracts many substances other than the emodin material, which might be weighed as emodin and similar compounds.

There is shown in the Table IV below numerous preparations each containing in each fluid ounce 4 grains of aloes, including the three recognized varieties, with the color reading which were obtained from them. The method is as follows:

Benzyl Alcohol Method—Analysis of Anthraquinones

1. (A) Place 10 cc. of the preparation in a separatory funnel, add 20 cc. of stronger ammonia water (28 per cent.), shake thoroughly for approximately five minutes. Let stand two hours, or more, shaking occasionally. Add 50 cc. of benzyl alcohol. Shake three or four minutes, shake occasionally before leaving work that day, and let stand over night. Draw off lower benzyl alcohol layer into glass-stoppered 100 cc. cylinder, which will give a volume of closely 65 cc. If this solution is slightly hazy due to moisture saturation and cold temperature a cubic centimeter of 95 per cent. alcohol will clear it up immediately. Add to residue in separatory funnel 25 cc. of benzyl alcohol. Shake occasionally during one hour and let stand until settled clearly, which approximately takes four or five hours. Draw off again lower benzyl alcohol layer into the same 100 cc. glass-stoppered cylinder. Make to volume with 95° alcohol. Shake and read color in ⅛-inch cell of the Lovibond tintometer.

1. (B) Take balance of the colored benzyl alcohol from the 100 cc. cylinder, which is 90 to 95 cc., and place in a 250 cc. beaker marked to a volume of 70 cc. Sink this in hole of steam bath with aid of beaker tongs and with a light current of air blowing over the beaker and steam on full. Evaporate to the 70 cc. mark. This will

TABLE IV

No.	Preparation containing 10 cc. used. 4 grains Aloes per fl. oz. in 40% Alc. A Direct extraction	Variety Socotrine B Ammonia driven off	⅛" cell used for all readings C Aqueous to 100 cc.
S-1	R—3.20 Y—1.40	R—2.62 Y—1.30	R— 4.70 Y—13.50
S-2	R—2.90 Y—1.20	R—2.30 Y—1.25	R— 4.50 Y—16.00
S-3	R—3.30 Y—1.20	R—2.62 Y—1.30	R— 4.40 Y—14.50
S-17	R—3.20 Y—1.40	R—2.50 Y—1.30	R— 3.50 Y—18.00
S-24	R—3.12 Y—1.20	R—2.30 Y— .70	R— 3.70 Y—13.50
S-14*	R—1.55 Y— .4	R—1.2 Y— .4	R— 5.3 Y— 4.4
	Curacao		
S-7	R—3.00 Y—1.70	R—2.50 Y—1.40	R— 3.80 Y—20.00
S-9	R—2.90 Y—2.00	R—2.50 Y—1.50	R— 3.90 Y—20.00
S-10	R—2.80 Y—2.00	R—2.30 Y—1.40	R— 4.50 Y—21.00
S-23	R—2.80 —1.30	R—2.30 Y—1.10	R— 4.40 Y—20.00
S-16	R—3.62 Y—2.00	R—3.12 Y—1.90	R— 3.62 Y—18.00
S-25	R—2.70 Y—1.50	R—2.40 Y—1.40	R— 3.30 Y—20.00
S-11	R—3.10 Y—2.20	R—2.70 Y—2.20	R— 3.12 Y—18.00
S-12	R—3.10 Y—2.20	R—2.70 Y—2.20	R— 3.10 Y—18.00
S-13	R—3.10 Y—2.20	R—2.70 Y—22.0	R— 3.30 Y—18.80
S-15	R—2.80 Y—2.00	R—2.50 Y—2.00	R— 3.50 Y—20.00

*Note—Analysis shows here from column "C" that the aloin in the above No. 14 has been practically all removed. This isolated sample which has been abnormal throughout was alleged to be Socotrine aloes.

CONTINUATION OF TABLE IV

No.	Preparation containing 10 cc. used. 4 grains Aloes per fl. oz. 40% Alc. A Direct extraction	Variety Socrotine B Ammonia driven off	⅛" cell used for all readings C Aqueous to 100 cc.	
		Cape		
S-4	R—1.45 Y—1.30	R—1.20 Y— .90	R— 3.70 Y—16.00	
S-5	R—1.85 Y—1.50	R—1.35 Y— .90	R— 3.70 Y—16.00	
S-6	R—2.00 Y—1.40	R—1.40 Y— .90	R— 3.80 Y—16.00	
S-21	R—1.65 Y—1.40	R—1.20 Y— .80	R— 3.40 Y—18.00	
S-18	R—1.85 Y—1.30	R—1.40 Y— .90	R— 3.30 Y—13.50	
S-26	R—1.65 Y—1.30	R—1.30 Y— .90	R— 3.00 Y—18.00	
S-20	R—1.68 Y—1.48	R—1.52 Y—1.40	R— 2.70 Y—12.40	
S-22	R—1.72 Y—1.40	R—1.52 Y—1.20	R— 3.10 Y—14.00	
		Aloin		
	(.02 gram in 10 cc. of 40% alcohol or .9 grain per fl. oz.)			
S-8	R— .60 Y— .70	R— .56 Y— .70	R— 1.50 Y—10.00	very old sample
S-27	R— .60 Y— .84	R— .60 Y— .80	R— 1.50 Y—11.50	new sample
S-28	R— .60 Y— .84	R— .60 Y— .80	R— 1.50 Y—11.50	new sample
	Commercial fluid Aloes of all U. S. P. varieties same equivalent Aloe amount used.			
73820	R—2.20 Y—1.60	R—2.00 Y—1.40	R— 3.50 Y—19.00	
73821	R—2.40 Y—1.60	R—2.40 Y—1.60	R— 3.20 Y—14.40	

NOTE—It will be observed from the following tables that the "C" column shows one of the most important parts of the analysis in that it is strongly indicative of the aloin content in the aloes used in that pure aloin shows a very high yellow reading and corresponding high yellow readings in all samples in "C" column. Below are given a few readings of other emodin bearing drugs and one made from a 1 per cent. caramel solution which also contains saffron and over twenty-five other non-emodin bearing drugs in solution.

	10 cc. used in all samples for analysis.		
	A	B	C
Rhubarb made up of 15 m. of F. E. per fl. oz.	R—3.70 Y— —	R—2.80 Y— .80	R—3.70 Y—3.70
Frangula made up of 30 m. F. E. per fl. oz.	R—4.00 Y— .64	R—2.80 Y—1.50	R—1.00 Y—1.00
Senna made up of 30 m. F. E. per fl. oz.	R—1.15 Y— .70	R— .95 Y— .70	R—4.12 Y—5.20
A 40% alcoholic solution containing saffron and small amounts of twenty-five non-emodin bearing medicinal herbs and 1% of N. F. V. caramel (no aloes present).	R— .44 Y— .74	R— .24 Y— .50	R— .40 Y— .84

remove all traces of ammonia. However, test with litmus paper for absolute removal of ammonia. The idea is to remove all ammonia from the solution. Remove from steam bath, cool, pour into a thoroughly dried 100 cc. glass-stoppered cylinder and make up to original volume placed in beaker with 95 per cent. alcohol, shake and read color in 1/8-inch cell Lovibond tintometer. We have found that this color is fairly permanent, lasting in intensity of color for quite a few months.

1. (C) The ammonical residue in separatory funnel is drawn into a 100 cc. cylinder, separatory funnel washed out with distilled water and added to solution in the cylinder and made up to the 100 cc. mark with water. Thoroughly mix and read color in 1/8-inch cell Lovibond tintometer.

NOTE: The benzyl alcohol used in all of our methods has been Eastman's chlorine free No. 40 benzyl alcohol. Just what cheaper grades, non-chlorine free benzyl alcohol will produce under such conditions cannot be vouched for, as so far they have not been tried. Although benzyl alcohol is considered an expensive reagent, at least three-fourths of the benzyl alcohol may be recovered by two simple distillations, one to remove alcohol, water and ammonia, and the second to purify it equal to its original state.

Phenolphthalein when mixed with samples analyzed did not in any way show up in the readings except in the "C" column where naturally the red color produced would make that column inoperative.

When Phenolphthalein is used for blanks in ammonical solution, the Benzyl alcohol, which carries down with it ammonia, water,

and some of the ethyl alcohol used in the samples, is absolutely colorless.

In order to furnish further data as to Column "C" being indicative of the aloin content in aloes, an experiment was made to that end by treating three different samples with Hydrogen Peroxide and analyzing as before with the following results tabulated both before and after. Ten cc. used for analysis in all cases.

	No. 28 aloin .02 gm. in 10 cc. 40% Alcohol.		No. 21 aloes made up 4 grains per fl. oz.		Commercial tonic sample alleged to contain 4 grains of aloes per fl. oz.	
	Before	After	Before	After	Before	After
A	R— .6 Y— .8	R— .4 Y— .5	R— 1.6 Y— 1.4	R—1.6 Y— .6	R— 1.5 Y— 1.1	R—1.2 Y— .8
B	R— .6 Y— .8	R— .3 Y— .6	R— 1.2 Y— .8	R—1.4 Y— .8	R— 1.3 Y— 1.2	R—1.0 Y— .8
C	R— 1.5 Y—11.5	R— .4 Y— .7	R— 3.4 Y—18.0	R—2.9 Y—5.0	R— 3.3 Y—11.5	R—2.0 Y—4.4

The Shaffer gravimetric analysis for aloin used in Europe is the most satisfactory method at present using 50 grams of aloes as outlined by the method. It becomes unreliable when applied to preparations containing aloes in 4 to 8 grain quantities per fluid ounce in the presence of other drugs and aromatics. It was found that various vegetable tonics entirely devoid of aloes or aloin or any emodin-bearing drugs will given even higher gravimetric results than on preparations containing just aloes in solution. Briefly the method is to take 50 grams aloes dissolved in hot weakly acid water, let stand over night, filter, make alkaline with ammonia and aloin precipitated with calcium chloride solution, the precipitate made slightly acid with HCl, the mass allowed to crystallize and filtered; washed with water saturated with aloin, dried and weighed as aloin. It is claimed that this method is more satisfactory for Curacao than for Socotrine or Cape aloes.

The Hager method which has also been used in Europe is practically worthless on preparations containing invert sugar or many other ingredients and is also unreliable when even applied to the pure aloes. This method depends, on a dry drug or extract, extracted with ether, then chloroform, or a mixture of Benzol, Chloroform

and absolute alcohol to remove other resinous bodies from aloes and then dissolved in alcohol 80 per cent. by volume, filtered, evaporated, taken up with water and diluted ammonia and precipitated by neutral lead acetate solution, this precipitate, water washed, is treated with ammonium sulphate and extracted with 80 per cent. alcohol, dried and weighed as aloes.

The once proposed A. O. A. C. method for the determination of total anthraquinones which were published with the previous articles on the emodin-bearing drugs have been omitted in this article for the reason that the residues obtained from aloes were very small (from .006 to .012 grams) and the color readings so weak as to be unsatisfactory.

The method is briefly 25 cc. of the tonic was extracted with 200 cc. of chloroform and dilute sulphuric acid, refluxed and then completely extracted with chloroform. This chloroform extracted with sodium hydroxide solution, the alkaline extracts made acid with hydrochloric acid and extracted with chloroform. Evaporate chloroform and weigh residue as total anthraquinone. This residue is further treated in turn by potassium hydroxide solution and then acid solution and the resulting colors produced red in a Lovibond tintometer.

In the chemical methods of the A. O. A. C. there is no method for the determination of aloin in aloes, but there has been recommended as tentative a method for aloin in crude aloin which is briefly as follows: A small quantity of aloin sample is dissolved in sodium hydroxide solution, made acid with sulphuric acid and extracted with chloroform. The aqueous solution is saturated with salt and shaken out with chloroform-alcohol mixture. This residue is taken as aloin and it is checked by acetylization with acetic anhydride and sodium acetate. It is extracted with chloroform and evaporated, multiplied by a factor and calculated as aloin.

This was recommended as a tentative method in the J. A. O. A. C. No. 18, 407, 1932, all other proposed methods for the determination of aloin in crude aloin having been temporarily rejected.

Another method for the determination of aloin in aloes known as the Briggs method which has been used, is to dissolve 50 grams of powdered aloes in boiling water and add acetic acid, mix and allow to cool, and filter. To the filtrate add lead acetate. Shake and filter. Remove lead with hydrogen sulphide. Concentrate clear filtrate to a small volume and allow aloin to crystallize at low temperature.

Conclusions and Suggestions

There is presented in the foregoing pages two colorimetric methods for the quantitative estimation of aloes in medicinal preparations, both of which are being used in the authors' laboratory.

These methods can and have been successfully used in the determination of aloes in crude aloes and could be used for the standardization of this drug.

It is suggested that only Curacao aloes be recognized as official by the U. S. Pharmacopœia and the methods outlined in this article be considered in its determination.

Much credit should be given to Mr. Loren Burritt for his assistance in many of these determinations.

Responsible persons may secure the names of the dealers and sources of the products used in this paper by addressing the authors' laboratory, Room 422, Treasury Building, Washington, D. C.

The Chemical Constitution of Fowler's Solution

Arsenious trioxide may react with potassium carbonate in accordance with any of the following equations:—

	1.00 gm. As_2O_3 liberate
1. $As_2O_3 + K_2CO_3 = 2KAsO_2 + CO_2$	0.2223 gm. CO_2
2. $2As_2O_3 + K_2CO_3 + H_2O = 2KH(AsO_2)_2 + CO_2$	0.1112 gm. CO_2
3. $As_2O_3 + K_2CO_3 + 2H_2O = 2KH_2AsO_3 + CO_2$	0.2223 gm. CO_2
4. $As_2O_3 + 2K_2CO_3 + H_2O = 2K_2HAsO_3 + 2CO_2$	0.4446 gm. CO_2
5. $As_2O_3 + 3K_2CO_3 = 2K_3AsO_3 + 3CO_2$	0.6669 gm. CO_2

The amount of carbon dioxide liberated from potassium carbonate by 1 gm. of arsenic trioxide has been determined by warming the arsenic with potassium carbonate and water in a current of nitrogen and passing the evolved gases, first through a drying tube and then through potassium hydroxide absorption bulbs. Eight determinations gave values ranging from 0.1098 to 0.1190 with an average of 0.1134 gm. of CO_2 liberated by 1 gm. of As_2O_3. This is in close approximation to the value of 0.1112 gm. required by equation (2) above, and so the arsenic appears to be present as potassium hydrogen meta-arsenite $KH(AsO_2)_2$; this confirms results obtained by other workers.—Jermstad and Ostby (*Pharm. Acta Helv.*, 1933, 7/8, 144, through *Phar. Journal.*)

UTILIZATION OF CARBOHYDRATES AND SALTS OF ORGANIC ACIDS BY C. DIPHTHERIAE IN THE PRODUCTION OF TOXIN OF HIGH Lf VALUE*

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THE recent advance in preventive medicine in respect to immunization against diphtheria, using toxoid and alum precipitated toxoid, demands a better and stronger antigen than was formerly deemed necessary.

Although some workers still prefer the coli-fermented media, the desire for a purer substrate has been uniform, and the attempts to grow the organism and produce toxin on a purely synthetic medium have been numerous.

Davis and Ferry (1) made an extensive investigation of toxin production and found, that with the media used it was necessary to have at least 10 per cent. meat infusion in order to produce toxin. Earlier workers, however, had reported toxin production on synthetic media, and Wadsworth and Wheeler (2) and later Kirkbride, Berthelsen and Clark (3) succeeded in producing toxin on a substrate containing lactate and solutions of inorganic salts, to which peptone and a small amount of dextrose was added. The toxin produced on this medium with a Park-Williams No. 8 strain of C. diphtheriae had an Lf value of ten to twelve units and proved suitable for toxoid production and for the immunization of horses. The addition of glucose as a source of energy was advocated by Spronck (4) and by Theobald Smith (5) and later by other workers (6), but in the continuous search for stronger toxin other sources of energy were investigated.

Hazen and Heller (7) reported that the addition of maltose enhanced the Lf value of the toxin produced on veal broth. Pope (8) tested the addition of glucose, fructose, galactose and various salts of organic acids to a synthetic medium of a somewhat similar composition as the one developed by Kirkbride, Berthelsen and Clark (3).

It is generally known that C. diphtheriae produces lactic acid when cultured in media containing glucose. It was, however, found in our work that not inconsiderable amounts of acetic acid were produced also, and therefore it was thought that the addition of sodium acetate to the medium might enhance toxin production, and

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at the same time increase the buffer action of the medium. Ramon and Berthelot (9), Pope (10), and Marbe, Dimitriu and Stefanesco (11) also recommend the addition of acetate, and the latter authors furthermore advocate the addition of still larger amounts of glucose than hitherto deemed suitable.

Ramon has stated that the flocculation (Lf) value of a toxoid is an expression of its antigenic activity. Some workers favor this view, while others do not accept it in all cases. Investigations which were carried out by us (12), and which are still in progress, seem to indicate that other factors may play an important role in the flocculation reaction, and that toxoids of high Lf value occasionally may be of inferior immunizing power. The tendency, however, is to use toxoids with as high an Lf value, but with as low a nitrogen content as possible, whether crude, purified or concentrated.

The desire to keep the nitrogen value low is due to the opinion that the occasionally severe reactions from the injection of toxoid are in some way connected with the organic nitrogenous constituents of the toxoid, but whether the reactions are due to specific or non-specific substances has not been settled.

It is to be surmised that the meat media which ordinarily are used contain large amounts of substances, which in no way are necessary for the development of antigenic activity by C. diphtheriae. When a basic medium for toxin production therefore has to be selected, the least complex one presumably should be favored.

The medium of Kirkbride, Berthelsen and Clark seems to meet this requirement; its composition is such that the peptone is the only factor of unknown composition; it has a nitrogen content of only 2.8 to 3.0 mg. N. per cubic centimeter; it is easily prepared in large quantities, and the toxins produced are fairly uniform in respect to m. l. d., L+ and Lf values.

The present work was undertaken to see if it were possible, using this medium as a base, to increase the potency of the toxin by the addition of different carbohydrates and salts of organic acids.

Experimental

The medium for toxin production was made exactly as described by Kirkbride and coworkers (3). One gallon bottles were used with an amount of 400 cc. of medium. The various solutions of carbohydrates and organic acids were sterilized separately and added with aseptic technic to each bottle to make the desired concentration, before

inoculation. A Park-Williams No. 8 strain of C. diphtheriae which had been transplanted daily over a period of many months on the same basic medium without any addition of carbohydrates, was used throughout the work as seed. The bottles were placed on the side in order to give a larger ratio of surface to volume than advocated by Kirkbride, Berthelsen and Clark. Incubation was carried out at 33 to 35 degrees C. for ten days. For the sake of brevity, only a few of the experiments made are tabulated in Table I.

TABLE I

Source of Energy	Final pH	Lf. units per cc.
Glucose 0.1%	8.2	11
" 0.2%	8.0	16
" 0.3%	7.8	15
Maltose 0.45%	7.8	18
Glucose 0.15% and Maltose 0.3%	8.0	20
" 0.2% " " 0.4%	8.0	20
Glucose 0.2% and Sod. Acetate 0.5%	8.2	20
" 0.2% " " " 0.75%	8.4	20
" 0.2% " " " 1.0%	8.4	20
Maltose 0.45% and Sod. Acetate 0.75%	8.4	32
" 0.45% " " " 1.50%	8.4	26
Sod. Acetate 0.75%	8.4	11
" " 1.5%	8.6	10
" " 2.25%	8.6	9
Sod. Acetate 0.5% and Sod. Succinate 0.1%	8.6	14
" " 0.5 and Sod. Succinate 0.1% and Maltose 0.3%	8.6	26
Sod. Succinate 0.5% and Maltose 0.45%	8.4	22

Discussion

It has been known for a long time that a good supply of oxygen is necessary for the production of toxin by C. diphtheriae. Aeration has been attempted, but the best results have been obtained when the ratio of surface (cm^2) and volume (cc.) of the medium is kept in the vicinity of unity; as stated by Pope (8), however, this value seems to vary for media of different composition. The optimum surface volume ratio of the medium in the culture bottles used in these experiments has been found to be about 0.75. This has been obtained by placing 400 cc. of media in gallon bottles, and incubating them in a horizontal position.

The optimum incubation time must also be determined for media of different composition, and under the experimental conditions stated, a definite increase in Lf units was found to take place if the time of incubation was extended from seven to ten days.

The Lf values obtained by the addition of glucose show the advantage of the increased surface volume ratio and the prolonged incubation. The addition of 0.1 per cent. of glucose gives as high a flocculation under the experimental conditions as formerly the addition of 0.2 per cent., but the optimum seems still to be 0.2 when this sugar is used.

Maltose has a distinct enhancing effect, which is evident in all cases where this carbohydrate is used. The combined addition of glucose and maltose to the basic medium used by us, does not give as high Lf value as that found by Hazen and Heller (7) where a broth medium was used, but the values we obtained with the two sugars combined are above those produced when each sugar was used alone.

Acetate as the only source of energy does not produce a satisfactory toxin. However, toxin of the highest Lf value was obtained by the addition of both sodium acetate and maltose to the basic medium. The optimum requirements were found to be the addition of 0.45 per cent. maltose and 0.75 per cent. sodium acetate, and it has been found possible to produce a uniform toxin regularly without any difficulty. This is of great importance in the routine work for the preparation of toxoid suitable for active immunization against diphtheria, and also in the production of antitoxin by horse immunization.

There has been a fairly close correlation between the Lf, m. l. d., and L+ values of the experimental toxins but this has not always been the case in regard to Lf values and immunizing power. The toxins which have been produced by the addition of 0.45 per cent. maltose and 0.75 per cent. sodium acetate to the infusion free base, have been found on the average to have an m. l. d. value of 0.001 cc. and an L+ value of 0.04 cc.

Succinate appears inferior to acetate in connection with maltose alone, but seems to be able to replace part of the acetate when used with maltose.

While working with the infusion-free medium we have found that the ratio between the m. l. d. and Lf values is different from the

one obtained with Martin's broth or fermented meat media. It was noted that fresh toxins made with the infusion-free medium, even at the peak of toxicity were less toxic than would be expected from the values obtained with the flocculation test, as compared with those of Martin's broth or fermented media.

Summary

1. Metabolism studies were made of C. diphtheriae when grown on semi-synthetic infusion-free medium. This was chosen because of its low nitrogen content and because of its ability to produce a uniform toxin in respect to m. l. d., L+ and Lf values. Various carbohydrates and salts of organic acids were added to the infusion-free medium, and their effects investigated. The optimal requirements were found to be the addition of 0.45 per cent. maltose and 0.75 per cent. sodium acetate.

2. A regular production of a uniform toxin is possible, with an m. l. d. of 0.001 cc., an L+ of 0.04 cc. and an Lf value of thirty-two to thirty-four units per cubic centimeter.

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ABSTRACTED AND REPRINTED ARTICLE

ON THE VITAMIN CONTENT OF COD-LIVER OIL, AS INFLUENCED BY THE NUTRITIONAL STATE OF THE COD* [1]

By E. Poulsson and F. Ender

(From the State Vitamin Institute, Oslo.)

IT IS a general conception that the vitamins of cod-liver oil are not synthesized in the organism of the cod, but are present in the food and simply stored in the liver. If this conception is right, a difference would be expected between the vitamin content of liver oil from well-nourished cod and liver oil from malnourished cod. These two types are represented on one side by the Newfoundland cod-liver oil, and on the other side by the Lofoten cod-liver oil, representing the main stock of the Norwegian production.

In Newfoundland the fisheries are carried out in July to September. At that time the spawning is finished, the cod is well fed on caplin and squid, the fish is plump and the liver large and contains 50 per cent. or more of oil.

Quite different are the conditions of life on the west coast of Norway, where the fishery takes place simultaneously with the spawning, *i. e.*, in January to April. When arriving at the coast from the Atlantic Ocean in January, the cod is in excellent condition, the stomach is filled with small fish and other sea animals, the liver is large and fat. At the spawning banks, however, millions and millions of fish are gathered in a relatively small space, the food is getting scarce, and the fat which is stored in the body and in the liver is drawn upon. Consequently the fish is getting leaner, the liver shrinks and its percentage of fat diminishes. "At the beginning of the season the cod which first arrive are very fat and have a high liver content,[2] while the spent fish every year are deprived of fats to the utmost limit." (Hjort 1914.) As a consequence of this inanition the yield of oil decreases, and simultaneously there is a shift in the ratio between the two vitamins, which will be described in detail in the following.

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[2] *I. e.*, the ratio between the weight of the liver and the weight of the fish.

Vitamin A

The biological testing of numerous samples of cod-liver oil is a laborious and tedious work, requiring a long time and an abundance of animals. Fortunately we have in the Carr-Price color reaction with antimony trichloride a convenient, rapid and, according to the opinion of most investigators, reliable method. Also according to our experience, based on a great bulk of material investigated in our Institute, the antimony trichloride values (blue units), with only few exceptions, run parallel with the biological A-values. The tests given below were carried out with the Rosenheim-Schuster tintometer, according to the directions for the use of this apparatus.[3] We emphasize that all the tests were made at practically the same temperature (16-18°).

Newfoundland Oils. The material consisted of forty-three samples from the years 1929-1931, transmitted through the general consulates of Montreal and New York or purchased in St. Louis. Most of them were in unopened original bottles and were kept in a cool and dark place. The average index of these forty-three samples was 10.8 blue units. This agrees well with the average found by Drummond and Hilditch (1930) for fifty-two Newfoundland oils, *viz.*, 10.86 blue units. A higher number is given by Davies (1930), who found an "average vitamin A index = 13.6." The technique used is not described.

Norwegian Oils. As regards the blue units the Norwegian oils showed lower figures. In the years 1930 and 1931 the average for 100 samples was 9.0.[4]

Vitamin D

For the quantitative determination of vitamin D, the method described by the author in collaboration with Lövenskiold (1928) was used, with the modification that the test period was prolonged from six to ten days. This gives the advantage that our results are comparable with those of many other investigators, who also use a test period of ten days.

The main features of our method are the following:

Preparatory period: The rats, at a weight of 40-50 g., are put on Steenbock and Black's rachitogenic diet 2965. After about sixteen

[3] Time limit 30 seconds.
[4] In 1932 for 53 samples 9.4.

to twenty-one days the rats are weighed for the second time, and under a light ether narcosis a radiograph is taken of the left knee joint. The degree of rickets is indicated by one to four plus signs. For the test period only rats with an advanced degree of rickets, *viz.*, three to four plus signs are used. The more advanced the disease is, the easier will be the quantitative estimation of the eventual recovery in the following period.

Test period: During the test period the animals are kept in individual cages. The oil to be tested is diluted with inactive peanut oil and is given directly into the mouth with a calibrated pipette. The activity of the oil is judged by comparing the radiographs at the beginning and at the end of the test period and is indicated by one to four plus signs; a thin line of calcification is indicated by +, two thin lines or a thick line by ++ etc. The commencing calcification sometimes fails to extend through the whole of the horizontal width of the metaphysis, leaving a gap in the middle, if so ½ is assigned to it. The degree of recovery in a batch of animals is found by dividing the total sum of plus signs by the number of animals for example

$2 + 2 + 1 + 1 + 3 + 2 = 11$, average recovery $\frac{11}{6} = 1.8$.

In our institute regularly many liver oils and other oils are investigated at the same time. To exclude the effects of suggestion the estimation (the comparison of the pictures) is always made by a person ignorant of the origin of the oil in the special case.

Norwegian Oils. The result of the tests of ninety-five samples, which the Institute received in the last couple of years, was that ninety-one of these oils showed an average healing of ++ (2.0) with a daily dose of 4 or 5 mg. (some of them even with a daily dose of 3 mg.).

Newfoundland Oils. Of the forty-three samples mentioned above on the average one and one-half to two times higher doses were required to attain the same result. Eighteen of these samples, which were received in the autumn of 1931, were first tested individually, then 10 cc. of each were put together. This average sample was tested in different doses. The result was as follows:

Dose in mg.	Number of rats.	Average healing.
5	17	1.2
7.5	41	1.7
10	17	2.6

This result checks well with the experiences of other investigators. In a booklet from the biological department of a Newfoundland cod-liver oil producer (Ayerst *et al.*, 1930) the following statement is made: "The criterion of vitamin D potency is a thin continuous line of calcification. A high grade of cod-liver oil produces this amount of healing with a 7.5 to 10 mg. daily feeding for ten days. We therefore have present in 7.5 or 10 mg. of cod-liver oil one unit of vitamin D, and the number of units per gramme (or 1000 mg.) is therefore 1000 divided by 7.5 to 10, or 133.3 to 100 units." A ten-day test period is fixed by the Wisconsin Alumni Research Foundation, and a total dose of 75 mg. This dose corresponds to a slightly higher daily dose than 7.5 mg. if the assay is made by our method. This is due to the difference between Steenbock's method and ours. According to Steenbock's method the total dose is mixed with a portion of the diet usually consumed by the rat in the course of the first six days. In this way a registration of the maximum effect is attained. By our method the individual doses are given to the very last day of the test period, and accordingly when the X-ray picture is taken, some of the effect is still latent. Steenbock's technique therefore in fact is more rational than ours.

Discussion

From the experiments recorded the conclusion can be drawn, that the liver oil from the spawning, malnourished cod contains a somewhat smaller amount of vitamin A but considerably more vitamin D than does the liver oil from the well-nourished not spawning cod.

The explanation of these seemingly paradoxical findings probably is that vitamin A is necessary for the maintenance of the body also for the adult fish (as for other vertebrates), and therefore the stores are consumed when the supply of food is scarce, while the vitamin D is not consumed by the mature animal, the skeleton of which is already completely developed. From an interesting paper by Hess, Bills and Honeywell (1929) it can be inferred that displacement of vitamin into the sex products is not the decisive factor, but the inanition *per se*. The material of those investigators consisted of cod kept for several months in a large sea-water tank, and during this time fed on very small amounts of flounder and cod. The fish was found to be practically in a starved condition, the livers were very small and poor in oil, but the smaller the livers (in relation to the body weight) and the

leaner they were, the more vitamin D contained the liver oil. From their summary we quote: "Contrary to the current opinion the antirachitic potency varies inversely with the amount of oil in the liver. From extremely "poor" livers oil was extracted which was 200 times more potent than high-grade cod-liver oil, and far more potent than any oil heretofore assayed." This is explained by Hess and his collaborators on the ground that "the fat is used up in the liver of the cod very much as Miescher and Greene found it to be consumed in the muscle of the salmon during the spawning period, when the fish takes practically no food. In the cod the antirachitic factor resists oxidation, remains behind and becomes concentrated in a liver that is shrunken and greatly impoverished." This experiment is repeated every summer at the west coast of Norway, but on a great scale and in a more lenient manner.

Summary

Liver oil from cod in inanition contains somewhat less vitamin A, but much more vitamin D than does the liver oil from cod in a well-nourished state.

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SOLID EXTRACTS

And now the lowly turnip reaches high estate. Turnip juice is the new vitamin-rich beverage offered as a depression substitute for orange juice or tomato juice.

Two pounds of ordinary raw turnips will give fifteen ounces of the juice, which is said to be sweet and not unpalatable. Salt improves the flavor, but for infants the pure juice is advised. The juice may be easily made at home by grating a section of turnip and pressing the juice from the minced material.

Heavy water, made by a very tedious process from ordinary water, concentrated by repeated electrolyses, is today available in laboratory quantities. It has a specific gravity of nearly 1.1 and while its therapeutic properties have not yet been studied something is known of its toxicity. Certain forms of animal life are promptly killed by it. In dilution it may have definite medicinal properties. It is given the chemical formula D_2O, D being the accepted symbol for heavy hydrogen or deuterium.

The ancients attributed marvelous curative powers to "the sweat of a toad." In China it is still used as an ingredient in the medicinal goulash which finds its way into those gigantic oriental pills or boluses.

Scientific workers have recently found that the external poison glands of toads secrete epinephrine, cholesterol, and ergosterol, compounds which certainly possess valuable therapeutic properties.

What makes the weeping willow weep? Heavy water perhaps! —For science has recently discovered that this tree, and many others retain "heavy water" which they take out of the general water supply, and build it into their woody tissues and into the starches and other carbohydrate foods they form. Although it is present only in very minute proportions in the normal water of the soil and of rivers, the willows are in some way able to select it out, so that a larger ratio of it is present in the water bound up in wood and carbohydrate than is present in the "normal" free water which the plant takes in.

A new centrifuge microscope is now available wherewith the observer can actually see cell contents propelled by centrifugal force.

This microscope is an ingenious example of combined optical and mechanical engineering. The specimen is whirled at rates up to 10,000 revolutions per minute and the observer, looking into the eyepiece, sees a clearly defined, stationary image like a motion picture, and he can watch the changes taking place in the living cells under such vigorous treatment.

Back to heavy water again. Too much of it in the body is now alleged to be not a manifestation of, but the cause of old age.

Cracking arteries, opaque eyes, grey hair or no hair, stooping shoulders,—all are said to be due to heavy water.

Because the human body evaporates a large portion of the water that it consumes, it will in the course of years become enriched with heavy water. The light water, evaporating at a lower temperature, leaves the body more readily than the heavy water.

The scientific observers conclude that "this increase in the proportion of heavy water in the body fluids may account for the increasing inhibitory action of the protoplasm during senility."

But nothing is said of ways and means of overcoming this senile density.

If Junior refuses to take his cod liver oil "straight," he probably will not object to eating it in a candy bar or ice cream, which he may soon be able to do as a result of recent investigations.

A method whereby the fresh cod livers can be mixed with cocoa in such a way that all the health-giving properties of the livers are retained without oiliness or objectionable taste or odor remaining has been recently developed at the Canadian Department of Fisheries. The new mixture can be successfully used in the manufacture of a chocolate confection.

Another testimonial for my lady nicotine! It has been lately discovered that the nicotine in the tobacco acts upon the suprarenal glands, causing them to discharge more suprarenin into the system. As a result, the glycogen stored in liver and muscles is converted to sugar, and the sugar concentration of the blood is increased.

The same thing happens after a meal. It is this increased sugar concentration that definitely relieves the fatigue and irritability which develop when the amount of sugar in the blood is at the fasting level, in other words, when you are hungry. This also explains why many tobacco users smoke when they feel tired or hungry. The nicotine relieves the hunger and fatigue temporarily by increasing the amount of sugar in the blood.

And the scientists who conducted these tests insist that they were not the "blindfold" kind of experiments.

Although radium was isolated more than thirty years ago, not more than 288.4 Gm. had been produced or imported in the United States up to the end of the year 1930. There has been no radium produced in the United States since 1926. The amount imported since then has increased, the imports in 1930 having amounted to 16.86 Gm. A recent report of the U. S. Bureau of Mines estimates that the exports of radium from the United States have not exceeded 20 Gm. and that the amount used in luminous materials since 1916 probably has not exceeded 30 Gm.

Dr. Alphonso D. Rockwell, the inventor of the electric chair, was himself opposed to capital punishment. When, however, the State of New York did not know how to work out the details of electrocution he came to her aid. As a leading practitioner in electro-therapeutics, he developed the crude electric chair and satisfied critics that the infliction of the death penalty by that means was painless. He died at the age of ninety-three.

Dr. Joseph Ignace Guillotin was a brilliant Paris physician of the eighteenth century. At his suggestion France adopted a machine for "humanely" beheading persons condemned to death to take the place of hanging or decapitation with the axe.

During the French Revolution he narrowly escaped being beheaded by the guillotine himself. He lived to an advanced age.

Execution by lethal gas as practised in Nevada was also proposed by physicians.

SCIENTIFIC AND TECHNICAL ABSTRACTS

Compiled by Arthur Osol, Ph. D.

The Reaction of Hydrogen Peroxide with Potassium Iodide and its Application to the Determination of Chromium. G. Hamann and R. Muller. *Arch. Pharm. 272,* 57-60 (1934). The results of a critical investigation of the iodometric method for the determination of hydrogen peroxide are reported. The method is shown to be accurate only when the solution of peroxide is acidified before the addition of potassium iodide. A solution of hydrogen peroxide containing 3.16% H_2O_2 assayed 0.35% when acidified ten minutes after the addition of potassium iodide, the results being still lower if the solution is alkaline when potassium iodide is added. The low results are attributed to the following reactions in neutral or alkaline solution:

$$KI + H_2O_2 = KIO + H_2O$$
$$KIO + H_2O_2 = KI + H_2O + O_2$$

This method of accelerating the decomposition of hydrogen peroxide is applied in the determination of trivalent chromium where an excess of the former is used to oxidize the latter to the hexavalent state. Ordinarily the excess of peroxide is slowly destroyed upon boiling but in the presence of potassium iodide in a slightly alkaline solution the decomposition is effected in one to two minutes. The solution is subsequently acidified and the chromium determined by titrating the liberated iodine.

The Determination of Arsenic in Medicinal Preparations. E. Kahane. *Journ. Pharm. et Chim. 19,* 116-123 (1934). The organic arsenical (0.2 to 0.4 gram) is treated with 5 cc. of a mixture of 700 cc. H_2SO_4 (1.81); 200 cc. $HClO_4$ (1.61) and 100 cc. HNO_3 (1.39) until the organic material is destroyed. Arsenic is converted to the pentavalent state by this treatment and is determined according to the procedure of Schulek and Villecz by reducing it to the trivalent form with hydrazine sulphate followed by reoxidation with N/10 $KBrO_3$. The excess of hydrazine sulphate is destroyed by boiling. Each cc. of N/10 $KBrO_3$ is equivalent to 0.00375 gram of arsenic. Excellent results were obtained in the determination of arsenic in 17 organic arsenicals (sodium cacodylate, stovarsol sodium, triphenylarsine, etc.).

A Note on the Chemotherapy of Experimental Tuberculosis of Guinea Pigs with Gold Compounds and Pregl's Solution of Iodine. J. A. Kolmer and H. Brown. *Journ. Chemotherapy, 10,* 73 (1934). Guinea pigs were inoculated with human tubercle bacilli and one week later were given treatments consisting of the injection of various gold compounds. The results of the experiments indicated that untreated controls and treated animals died within an average of 40 days after infection. One animal receiving gold monoiodide lived 73 days, while another receiving gold thiosalicylic acid lived 65 days, however necropsy showed wide-spread tubercular lesions. The following compounds were ineffective in treating experimental tuberculosis in guinea pigs: gold monoiodide, gold thiosalicylic acid, gold guaiacol, gold thiourea, gold p-thiocresol, quinine aurothiosulphate, and sodium aurothiosulphate. Similar experiments with Pregl's iodine solution also gave negative results.

A Molecular Compound of Pyramidon and Diallylbarbituric Acid. P. Pfeiffer and E. Ochiai. *Journ. prakt. Chem. 74,* 335 (1933). Pfeiffer and others have shown that many drug combinations are molecular compounds, the molecular ratio in all of the cases investigated being 1 : 1. Examples of such compounds are those of pyramidon and voluntal, pyramidon and butychloral hydrate, antipyrin and chloral hydrate, and pyramidon and veronal. The authors show that pyramidon and diallylbarbituric acid likewise form a compound in the molecular ratio of 1 : 1. The compound consists of slightly yellowish crystals which soften at 92.5° C. and melt completely at 131° C. Melting is non-homogeneous, indicating partial decomposition into the two components.

The Determination of Aldehydes other than Citronellal. Report of the Essential Oil Sub-Committee to the Standing Committee on Uniformity of Analytical Methods (Society of Public Analysts). *Analyst. 59,* 105-108 (1934). The investigations of the Sub-Committee have shown that, for the determination of aldehydes in essential oils, the hydroxylamine method offers considerable advantages over the commonly employed bisulphite and neutral sulphite methods. This method is a definite determination of aldehydic (or ketonic)

substances, and is affected very little, if at all, by the presence of traces of free organic acids such as are frequently present in essential oils, as these are usually without action on the indicator used in the method.

The method consists in weighing out exactly, in a glass-stoppered tube—approximately 150 mm. long by 25 mm. in diameter—a suitable quantity of oil, adding 5 cc. of benzene and 15 cc. of N/2 hydroxylamine hydrochloride reagent. After vigorous shaking the mixture is titrated with N/2 alcoholic potash until the red color changes to yellow. The titration is continued until the full yellow color of the indicator is permanent in the lower layer after shaking vigorously for two minutes and then allowing to stand for the liquids to separate. The result should be confirmed by a second determination. The number of cc. of N/2 alcoholic potash used multiplied by the correcting factor 1.08, by the factor for the appropriate aldehyde, and by 100, and divided by the weight of oil taken will give the percentage (by weight) of aldehydes, calculated as that aldehyde, present in the oil. To prepare hydroxylamine hydrochloride reagent, dissolve 3.475 grams of the pure crystals in 95 cc. of 60% alcohol, add 0.5 cc. of 0.2% methyl orange indicator, adjust to the full yellow color of the indicator with N/2 alcoholic potash and make up to 100 cc. with 60% alcohol.

A Rapid Method for the Accurate Determination of Minute Quantities of Nitrite. G. G. Rao and K. M. Pandalai. *Analyst. 59,* 99-100 (1934). The essential reaction in the proposed determination is:

$$2HNO_2 + 2HI = 2H_2O + I_2 + 2NO$$

To prevent high results being obtained, two conditions must be fulfilled: (1) There must be no dissolved oxygen in the reaction mixture, and the atmosphere over the solution must consist of carbon dioxide. This condition is secured by causing a rapid stream of carbon dioxide to bubble through the solution for about ten minutes. (2) The nitric oxide must be expelled from the system as it is liberated. For this purpose some sodium bicarbonate is added to the reaction mixture at the outset. In making a determination, 20 cc. of the nitrite solution are placed in a 250 ml. flask, into which are then introduced about 4 grams of sodium bicarbonate, 5 ml. of 10% potassium iodide solution, and a little starch solution. Next, a rapid stream

of purified carbon dioxide is made to bubble through this reaction mixture in the flask for about 10 minutes to ensure the complete removal of oxygen. The solution is then acidified with 10 ml. of 5 N oxygen-free sulphuric acid, and the liberated iodine titrated with N/500 sodium thiosulphate solution. Each ml. of thiosulphate is equivalent to 0.000028 gram of nitrite nitrogen. The average error is reported to be 0.25%.

Action of Ultra-Violet Light on Alkaloids. Q. Mingoia. *Ann. Chim. appl., Roma. 23,* 318 (1933). Through *Quart. Journ. Pharm. Pharmacol. 6,* 669 (1933). Solutions of the hydrochlorides of diamorphine, cocaine and codeine, and of atropine sulphate were subjected to irradiation from a mercury lamp. Where the solutions were in a quartz container, or the light was allowed to fall on the surface without passing through the walls of the container, rapid decomposition was observed; solutions in glass bottles were unaffected. When the solutions were subjected to Wood's light they were unaffected. To see whether it would be possible to sterilize solutions of these alkaloids, which are damaged by heat, by exposing to Wood's light, the solutions were infected with cultures of various fungi and bacteria and then subjected to Wood's light for one or two hours, but the sterilizing effect was negligible.

Identification of Arsphenamine and Neoarsphenamine. M. Wagenaar. *Pharm. Weekbl. 70,* 597 (1933). Through *Quart. Journ. Pharm. Pharmacol. 6,* 669 (1933). When a small quantity of arsphenamine is placed on an object glass, and covered with a cover glass, supported on a glass ring, on which is placed a drop of furfural and a trace of pyridine, the yellow grains of the arsphenamine are observed to change into blue-black drops. This reaction is not produced by neoarsphenamine, and can be used microscopically to show the presence of arsphenamine in neoarsphenamine. For the development of the color it appears necessary for the amino group to be combined with an acid, as neoarsphenamine gives a similar color if treated with hydrochloric acid.

MEDICAL AND PHARMACEUTICAL NOTES

The Tannic Acid Treatment of Burns

Since the tannic acid treatment of burns became known here, a large number of physicians, particularly in the "accident hospitals," have adopted this method. In order to bring the method to the attention of more physicians, a number of lectures and demonstrations on the subject were held at a recent session of the Vienna Medical Society. It was stressed that the chief advantage of this method holds not so much for adults as for the burns of children, whose lives are thereby saved; for ordinarily the prognosis in the case of children with burns is much more unfavorable than with adults. The new method reduces the pain and dispenses with bandages and the use of the protracted water bath. In combination with blood transfusion and injections of sodium thiosulphate, the results have been excellent. Of all the methods recommended for the use of tannic acid, the following has proved to be the most effective: Moistening or spraying of the burned portions of the body, every quarter of an hour, with a 2.5 per cent. solution, over a period of from twelve to eighteen hours. As soon as the crust has formed, the patient needs little further care. The crude tannic acid is superior to the purified, and the best effects are secured if the solution is applied at a temperature of 30 C. (86 F.). The stay in the hospital is reduced at least 20 per cent. Scar formation and contractures are much more rare and more pliable than formerly. The sooner the tannic acid is applied, the better the results. The mortality has been reduced from 13.5 per cent. to 2.4 per cent., whereas with the trinitrophenol therapy formerly employed the mortality ranged from 11 per cent. to 40 per cent.—*Jour. A. M. A. 102,* 8, p. 632.

Medicinal Whisky

The Federal Food and Drug Administration issued a statement, February 16, calling attention to the requirements of the Food and Drug Act concerning medicinal whisky as differentiated from a product intended exclusively for beverage use. Under the law, drugs listed in the U. S. Pharmacopœia must conform to the definition in that authority and in the case of whisky the definition is more

rigid than that for "straight whisky," recently issued by the Federal Alcohol Control Administration. Pharmacopœia whisky must be aged at least four years in charred wood containers and its alcoholic content must be not less than 47 per cent. and not more than 53 per cent. by volume of absolute alcohol. A product varying from these specifications may be sold, if the label carries a statement of the strength, quality and purity, but it must be marked "Whisky not U. S. P." Diluted alcohol, with or without artificial flavor and color, cannot be sold under the name "whisky," no matter how that name may be modified or qualified. Such a compound may be sold as a drug under a name other than whisky, if the name is not false or misleading in any particular. The announcement is not to be construed as modifying or changing the regulations of the Federal Alcohol Control Administration relative to the labeling of distilled spirits but shall be considered as an addition thereto, it was emphasized.

Stability of U. S. P. Ether After the Metal Container Is Opened

1. U. S. P. ether in metal cans, as it is supplied in this country at the present time by the better known manufacturers, does not deteriorate rapidly under ordinary conditions when the metal containers are opened. The present study shows that the can may be opened and again stoppered with cork many times during periods of weeks without oxidation detectable by the U. S. P. tests.

2. There is no evidence that ether specially purified "for anesthesia" has any material advantage over ordinary U. S. P. ether for anesthetic purposes.

3. It is recommended that hospitals buy ordinary U. S. P. ether in large steel drums and that for anesthesia the operating room be supplied with ether in small tin cans filled daily from the drums by the hospital pharmacist. The ether in the drum may be tested daily for aldehydes and peroxides, there being very simple tests for each requiring only from five to ten minutes to perform. This would help not only to correct an erroneous view regarding the speed of deterioration of ether after the container is opened, but to abolish the extravagant practice of buying ether in hundreds of quarter-pound or half-pound cans at from four to six times the cost of ether in drums, when large quantities of ether for anesthesia are used.—(H. and D. Gold), *Jour. A. M. A. 102*, 11, p. 819.

Formulas Proposed for the British Pharmaceutical Codex

UNGUENTUM METHYLIS SALICYLATIS COMPOSITUM.—*Synonyms.*—Unguentum Methylis Salicylatis Compositum Forte; Strong Compound Ointment of Methyl Salicylate; Unguentum Betulæ Compositum; Unguentum Analgesicum; Analgesic Balsam.

Methyl Salicylate	50.0 g.	2 oz.
Menthol	10.0 g.	175 gr.
Eucalyptol	2.5 g.	43¾ gr.
Oil of Cajuput	2.5 g.	43¾ gr.
White Beeswax	20.0 g.	350 gr.
Hydrous Wool Fat	15.0 g.	262½ gr.

UNGUENTUM POTASSI POLYSULPHIDI.—*Synonyms.*—Marcussen's Ointment; Danish Ointment.

Potassium Hydroxide ..	12.5 g.	½ oz.
Sublimed Sulphur	12.5 g.	½ oz.
Yellow Soft Paraffin ...	22.5 g.	393¾ gr.
Wool Fat	22.5 g.	393¾ gr.
Zinc Sulphate	2.8 g.	49 gr.
Sodium Hydroxide	0.8 g.	14 gr.
Distilled Water	15.7 ml.	302 m.
Benzaldehyde	0.5 ml.	10 m.
Liquid Paraffin	to 100.0 g.	to 4 oz.

Dissolve the potassium hydroxide in an equal weight of water, add the sulphur, boil gently until dissolved and mix the solution with the yellow soft paraffin and the wool fat. Dissolve the sodium hydroxide in the remainder of the distilled water, add the zinc sulphate, shake well, and incorporate the mixture with the ointment; then add the benzaldehyde and sufficient liquid paraffin to produce the required weight.

Metycaine

Benzoyl-γ-(2-methylpiperidino)-propanol hydrochloride. —γ-(2-methylpiperidino)-propylbenzoate hydrochloride.

$$-C_6H_4.COO(CH_2)_3.NC_6H_{12}.HCl.-$$

The base of metycaine differs from the base of procaine hydrochloride in having the basic nitrogen in a methylpiperidino ring instead of the

dimethylamine, a propanol group in place of the ethanol group, and in not having an animo group attached to the benzene ring. In addition, it possesses an asymmetrical carbon atom and is optically inactive. Metycaine is therefore a racemic mixture of the hydrochlorides. It is manufactured by Eli Lilly & Co.

Actions and Uses.—Metycaine is a local anesthetic, which produces prompt anesthesia either by subcutaneous injection or topical application to mucous membranes and similar surfaces. Pharmacologic studies on animals indicate that the toxicity of metycaine following subcutaneous injection is lower than that of cocaine and comparable to that of procaine; intravenously, it was found to be approximately three times as toxic as procaine.

Dosage.—For application to the eye, metycaine is used in 2 per cent. solutions; for nose and throat, 2 to 10 per cent. solutions are used; 1 to 4 per cent. solutions have been used for urethral anesthesia; for infiltrative anesthesia in small areas, solutions of 0.5 to 1 percent. are generally used.—*Jour A. M. A.*, Feb., 1934, p. 456.

Announcing Reprints of "The Professional Pharmacy"

The second report from the prescription department phase of the National Drug Store Survey of the Bureau of Foreign and Domestic Commerce, U. S. Department of Commerce, entitled *"The Professional Pharmacy,"* was published in the July, August, September and October issues of the *Journal of the American Pharmaceutical Association.*

This report, by Frank A. Delgado and Arthur A. Kimball, has been reprinted in pamphlet form by the Association, making it available to all branches of the profession and industry. Copies may be obtained from the Association at 25 cents each. A discount of 10 per cent. is given in lots of 6 or more copies, 20 per cent. in lots of 100 or more, and 25 per cent. in lots of 250 or more.

This report should be of great value to all branches of pharmacy, because it gives much practical information of interest to the proprietors of professional and commercial type pharmacies, professors and students in colleges of pharmacy, manufacturers and wholesalers of pharmaceuticals, etc., and others. Many complimentary letters have been received concerning the report. Some colleges of pharmacy

have ordered copies for their students, using the publication as a textbook. Manufacturers and wholesalers are ordering them for the use of their agents and customers.

The publication not only presents the findings of the intensive survey, but makes practical suggestions for improvement in pharmaceutical practice. Among the subjects covered are the following: Fixture and prescription inventory requirements in opening a new store. Sales, expense and prescription business in the professional pharmacy. Prescription business by type of prescription in 1910, 1920 and 1930. Seasonal demand for prescriptions. Prescription price trends by type and nature of prescription. Changing price trends in 1910, 1920, and 1930. Inconsistency in prescription pricing; prescriptions priced below cost. Average cost of materials in prescriptions. Prescription business according to the physicians writing the prescriptions. Preference of physicians for official or specialty remedies. Prescription inventory problems and ingredient analysis. Opening business and extent of growth of a drug store's prescription business. Frequency of occurrence of ingredients. Private formula prescriptions. Simplification of the prescription department inventory. Introduction of new manufacturers' specialties. Lists of the leading ingredients based on study of 20,000 prescriptions.

The first report on the professional phase of the National Drug Store Survey was entitled: "Prescription Department Sales Analysis in Selected Drug Stores," and was by the same authors. The American Pharmaceutical Association also cooperated with the U. S. Department of Commerce in the preparation of this first report, which can be obtained from the Superintendent of Documents, Washington, D. C.